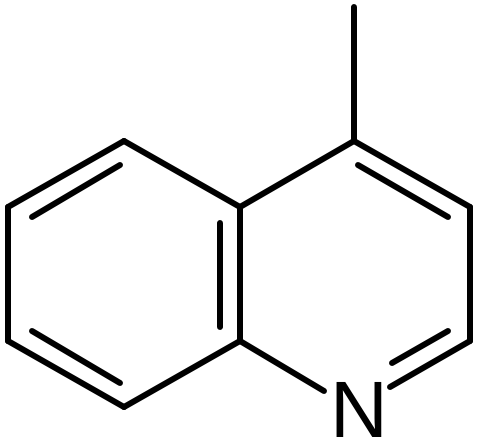
# 4-Methylquinoline
# (4-MeQ)




**Molecular Weight: 143.19  CAS Reg. No.: 491-35-0**

# 4-Methylquinoline Use/Occurrence

- **No known uses**
- **Environmental contaminant**
- **Associated with:**
  - Shale oil and coal gasification
  - Wood treatment
  - Tobacco smoke
  - Urban particulate matter

# Carcinogenicity of 4-MeQ

- **Carcinogenicity in humans:**
  - No data
- **Carcinogenicity in experimental animals:**
  - Intraperitoneal injection studies in mice (LaVoie *et al.*, 1988)
  - Subcutaneous injection studies in rats (LaVoie *et al.*, 1988)



# Tumors in Mice (LaVoie *et al.*, 1988)

**Newborn CD-1 mice injected 3 times intraperitoneally**

| Treatment | Sex | Liver tumors | | | Lung tumors |
|---|---|---|---|---|---|
| | | Total | Adenomas | Hepatomas | |
| **4-MeQ** | Male | 23/28 * | 20/28 * | 3/28 | 2/28 |
| | Female | 0/29 | 0/29 | 0/29 | 2/29 |
| **Control (DMSO)** | Male | 4/21 | 0/21 | 0/21 | 0/21 |
| | Female | 0/21 | 0/21 | 0/21 | 0/21 |

* Significant increase over controls ($p < 0.0001$).



# Tumors in Rats (LaVoie *et al.*, 1988)

**Newborn Sprague-Dawley rats injected subcutaneously**

| Treatment | Sex | Liver tumors | | |
|---|---|---|---|---|
| | | Total | Adenomas | Hepatomas |
| **4-MeQ** | Male | 1/26 | 0/26 | 1/26 |
| | Female | 2/20 | 2/20 | 0/20 |
| **Control (DMSO)** | Male | 5/27 | 3/37 | 2/27 |
| | Female | 1/22 | 1/22 | 0/22 |



# Mouse Dermal Initiation/Promotion Studies
## (LaVoie *et al.*, 1983 & 1984)

**Skin tumor incidence in SENCAR mice treated dermally**

| Study | Initiating Dose of 4-MeQ | Promoting Dose of TPA | Evaluation Period (following promotion) | Skin Tumor Incidence |
|---|---|---|---|---|
| LaVoie et al., 1983 | 5 mg | 150 µg over 20 wk | 20 wk | 11/25 * |
| | 0 | 150 µg over 20 wk | 20 wk | 1/24 |
| LaVoie et al., 1984 | 7.5 mg | 72 µg over 18 wk | 18 wk | 13/29 * |
| | 0 | 72 µg over 18 wk | 18 wk | 3/39 |

* Significantly increased relative to controls ($p<0.05$)



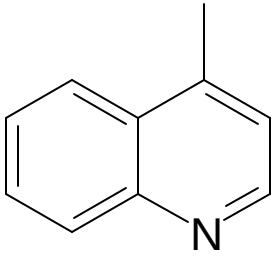
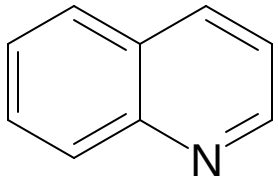
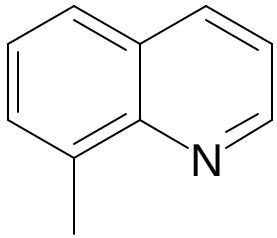


# Genotoxicity of 4-MeQ

- **Bacterial assays**
  - Consistently positive in *Salmonella* reverse mutation assays in the presence of metabolic activation
  - Single report of a positive forward mutation assay in *Salmonella*
  - Induction of unscheduled DNA synthesis in rat hepatocytes



# Structure-Activity Comparisons

| 4-Methylquinoline | Quinoline | 8-Methylquinoline |
|---|---|---|
|  |  |  |
| Liver tumors<br>Initiating activity | Vascular tumors (liver)<br>Liver tumors<br>Initiating activity | Liver tumors<br>Initiating activity |

# 4-MeQ: Summary

- **Animal evidence of carcinogenicity:**
  - Induction of liver tumors in male mice following intraperitoneal injection
- **Other relevant evidence:**
  - Initiation activity in initiation/promotion studies
  - Genotoxicity
  - Structure-activity analogies